



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/552,272	04/19/2000	Li Fang	1113CIP4PCTUS00	3198
35811 7590 07/27/2007 IP GROUP OF DLA PIPER US LLP ONE LIBERTY PLACE 1650 MARKET ST, SUITE 4900 PHILADELPHIA, PA 19103			EXAMINER EPPS FORD, JANET L	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 07/27/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	09/552,272	FANG ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 July 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: _____.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see the attached reply to Applicant's arguments.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit: 1633

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 112

2. Claims 52, and 54-55 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record.
3. Applicant's arguments filed 7-02-07 have been fully considered but they are not persuasive.

Applicants traverse the instant rejection on the following grounds:

"[T]he Applicants respectfully submit that it is well known in the art to use a vector with regulatory sequence elements to control the expression of an inserted heterologous gene in a host organism. A heterologous gene is defined in the art as a gene originating from an organism of another species.

Claim 52 recites an expression vector that includes a heterologous gene specifically regulated by the sequence elements of SEQ ID NOs: 49, 50, or the particularly recited portions of SEQ ID NO: 55. Therefore, contrary to the suggestion in the Official Action, the claim is not drawn to a gene regulated by a mechanism other than the sequence elements of SEQ ID NOs: 49, 50, or the particularly recited portions of SEQ ID NO: 55.

Furthermore, Claim 52 does not recite any sequence encoding a cold-shock inducible gene or any gene regulated by cold-shock sequence elements, but rather pertains to the expression of a heterologous gene inserted into a vector. Simply by nature of being inserted into a vector containing the elements recited in Claim 50, the heterologous gene becomes a cold-shock inducible gene that is regulated by cold-shock sequence elements. Therefore, the structure of a gene potentially regulated by the cold-shock sequence elements is merely a matter of insertion of a heterologous gene into a vector that contains such regulatory elements. Indeed, the heterologous gene of the rejected claims may be derived from any organism other than *E. coli* and is not necessarily associated with cold-shock in its normal expression pattern."

Contrary to Applicant's assertions, the instant claim 50, lines 1-2, clearly recite "a vector capable of expressing a heterologous gene in a bacterium at ***physiological temperature*** or under conditions that elicit a cold shock response comprising...." Claim 52, which dependent from claim 50 recites the vector of claim 50, *further comprising a coding region....* wherein said coding region comprises a coding region of a heterologous gene and is ***regulated*** by said regulatory elements. The scope of the term regulated as recited in the instant claims is not specifically limited in any manner. Therefore, the scope of the term is interpreted broadly, as encompassing any manner of regulation. The structures of *E. coli* cspA, cspB, and the csdA genes, are set forth in the specification as filed, and in the prior art as of the filing date of the instant specification. However, other than the cspA, cspB, and the csdA genes, neither the specification as filed, nor the prior art, provides a sufficient description of the full scope of nucleic acid sequence structures encoding cold-shock inducible genes, or genes that are regulated by some other mechanism by SEQ ID NO: 49, 50 or particularly recited portions of SEQ ID NO: 55.

Moreover, the specification (bridging paragraph of pages 22-23) as filed teaches that : "[t]he 5' untranslated region (5' UTR) of the mRNA of the *E. coli* cold-shock protein, CspA, contains a region immediately 5' to the Shine-Dalgarno region which is susceptible to degradation, presumably by RNAase E, at physiologic growth temperatures of about 37.degree. C. Therefore, the cspA mRNA containing the 5' UTR is unstable under normal growth conditions, having a half life estimated to be

approximately 12 seconds. Other cold-shock proteins, such as *E. coli* CspB and CsdA, are similarly unstable at physiologic growth temperatures due to instability of their mRNA. Upon cold shock, such as when the temperature is reduced to 15.degree. C., the half life of the cspA mRNA increases dramatically, to about 15 minutes, an increase in stability of about 75 times over the mRNA at normal physiologic growth temperatures."

The disclosure of the specification teaches that the cspA mRNA is unstable at physiological temperature, however it is stable when the temperature is reduced to 15°C. Without knowledge of the stability of the various mRNA transcripts produced by the heterologous genes encompassed by the claims, it is unclear how the skilled artisan would be able to predict whether or not the regulatory elements recited in the claims would be able to "regulate" in an undefined manner, the heterologous genes encompassed by the instant claims.

Since there is no clear correlation between the structures of genes that are potentially regulated by these sequence elements, the skilled artisan is left to further *de novo* experimentation to discover the full scope of nucleic acids that function as cold-shock inducible genes, or genes that are regulated by the sequence elements recited in the instant claims. As stated in the prior Office action, MPEP § 2163: "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

Conclusion

4. Claims 1, 5-6, 10, 14-19, 23-28, 32-37, 50 and 53 are allowable.
5. Claims 52, and 54-55 remain rejected for the reasons set forth above.
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE